Preplanned Studies

Prevalence of Metabolic Dysfunction-Associated Steatotic Liver Disease with Clinically Significant Fibrosis in Obese Patients with Type 2 Diabetes Mellitus — China, 2017–2024

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Summary

What is already known about this topic?

Metabolic dysfunction-associated steatotic liver disease (MASLD) with clinically significant fibrosis substantially elevates the risk of liver-related complications and mortality. The American Diabetes Association consensus report specifically recommends systematic risk stratification for MASLD and hepatic fibrosis in patients with type 2 diabetes mellitus (T2DM), with particular emphasis on those presenting with obesity.

What is added by this report?

This multicenter study demonstrates that obese patients with T2DM exhibit a substantially elevated prevalence of MASLD with clinically significant fibrosis compared to their non-obese counterparts (26.7% *vs.* 8.4%). Furthermore, the prevalence escalates progressively with the accumulation of cardiometabolic risk factors, highlighting the synergistic impact of multiple metabolic abnormalities on hepatic fibrosis development.

What are the implications for public health practice?

Our findings underscore the critical need for routine screening and integrated management of MASLD with clinically significant fibrosis in patients with T2DM, particularly those presenting with obesity and multiple cardiometabolic risk factors.

ABSTRACT

Introduction: This study investigated the prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) with clinically significant fibrosis among obese patients with type 2 diabetes mellitus (T2DM).

Methods: This multicenter study enrolled T2DM patients from tertiary hospitals and primary care facilities across 21 cities in China between 2017 and 2024. Clinically significant fibrosis was defined as liver stiffness measurement (LSM) ≥8 kPa assessed by vibration-controlled transient elastography (VCTE) or biopsy-confirmed fibrosis stage ≥F2.

Results: Of the 10,281 patients included, 9,725 comprised the VCTE cohort (5,171 from clinics and 4,554 from primary care), while 556 comprised the biopsy cohort. Overall, 25.6% were obese. The prevalence of MASLD with clinically significant fibrosis reached 26.7% in obese patients, significantly exceeding that in non-obese patients (8.4%). This prevalence increased progressively with rising body mass index and demonstrated a strong association with the number of cardiometabolic risk factors. Furthermore, a non-invasive model incorporating age, waist circumference, alanine aminotransferase, total bilirubin, and triglycerides exhibited reliable performance in stratifying the risk of MASLD with clinically significant fibrosis among obese patients with T2DM [Area under the receiver operating characteristic curve (AUC): 0.799 (95% *CI*: 0.767–0.832)].

Conclusions: MASLD with clinically significant fibrosis is highly prevalent among obese patients with T2DM, emphasizing the necessity for systematic risk stratification and integrated management of these interconnected metabolic conditions.

Metabolic dysfunction-associated steatotic liver disease (MASLD) affects approximately 38% of the global adult population, with its prevalence rising in parallel with the growing burden of metabolic disorders (*1*). The progression to clinically significant

fibrosis substantially elevates the risk of liver-related complications, including cirrhosis and hepatocellular carcinoma (*2*). Cardiometabolic risk factors (CMRFs), particularly type 2 diabetes mellitus (T2DM) and obesity, frequently coexist with MASLD and further accelerate disease progression (*3*). Recognizing this critical intersection, the recent American Diabetes Association (ADA) consensus report recommends systematic risk stratification for MASLD and liver fibrosis in adults with T2DM, especially those with obesity (*2*). Despite these recommendations, comprehensive prevalence data and risk factor analyses for MASLD with clinically significant fibrosis among patients with both obesity and T2DM in China remain scarce. To address this knowledge gap, we conducted a large-scale multicenter study to evaluate the prevalence of MASLD with clinically significant fibrosis in obese patients with T2DM and to identify associated risk factors. Additionally, we systematically examined how five CMRFs, individually and in combination, contribute to the development of clinically significant fibrosis in this high-risk population.

This prospective multicenter study enrolled adult patients with T2DM from tertiary hospitals and primary care facilities across 21 cities in China (Supplementary Table S1, available at https://weekly.chinacdc.cn/). The study comprised two cohorts: the vibration-controlled transient elastography (VCTE) cohort included patients who underwent VCTE examination between 2022 and 2024, while the liver biopsy cohort included patients with MASLD and T2DM who underwent liver biopsy between 2017 and 2024 (Supplementary Figure S1, available at https://weekly.chinacdc.cn/). All VCTE examinations were performed using the FibroScan® device (Echosens, Paris, France) according to standardized protocols. Clinically significant fibrosis was defined as liver stiffness measurement (LSM) ≥8 kPa in the VCTE cohort or histological fibrosis stage ≥F2 in the biopsy cohort, consistent with our previous study (*4*). Statistical analyses were conducted using SPSS (version 27.0.1, IBM SPSS Statistics, Armonk, NY, USA) and GraphPad Prism (version 10.0; GraphPad Software, San Diego, CA, USA). Additional methodological details, including exclusion criteria, VCTE reliability standards, histological assessment procedures, and statistical methods, are provided in the Supplementary Materials (available at https://weekly.chinacdc.cn/).

A total of 10,281 participants were enrolled from two cohorts. The VCTE cohort comprised 9,725 participants (50.0% male; 24.5% obese). Obese patients were younger than their non-obese counterparts [49.4 (14.34) *vs.* 56.6 (13.18) years] (Table 1). Of these, 5,171 patients were recruited from clinics and 4,554 from primary care settings. Patients in primary care were older [61.4 (10.39) *vs.* 49.0 (13.87) years] and had a lower obesity prevalence (16.6% *vs.* 31.5%) compared to those in clinics (Supplementary Table S2, available at https://weekly.chinacdc.cn/). The liver biopsy cohort included 556 biopsy-proven MASLD patients with T2DM (48.9% male; 44.1% obese) (Table 2).

In the VCTE cohort, the overall prevalence of MASLD, MASLD with clinically significant fibrosis, advanced fibrosis, and cirrhosis in T2DM patients was 59.7%, 13.0%, 6.8%, and 3.1%, respectively (Figure 1A). Obese patients with T2DM demonstrated significantly higher prevalence rates across all fibrosis stages compared to non-obese patients with T2DM, with MASLD with clinically significant fibrosis at 26.7% *vs.* 8.4% (P<0.001) (Figure 1B).

The prevalence of MASLD with cirrhosis in obese T2DM patients was higher in clinics than in primary care (Figure 1C). Non-obese T2DM patients in clinics exhibited lower prevalence rates of MASLD, clinically significant fibrosis, and advanced fibrosis compared to those in primary care (Figure 1D). Notably, MASLD and fibrosis prevalence increased progressively with body mass index (BMI), reaching the highest levels in obese patients compared to underweight, normal weight, and overweight groups (Supplementary Figure S2A, available at https://weekly.chinacdc.cn/). Moreover, among obese patients, applying different BMI cutoff values to define obesity classes revealed generally similar trends (Supplementary Figure S2B).

Sensitivity analyses using alternative definitions of central obesity yielded results consistent with those based on BMI-defined obesity, confirming higher MASLD and fibrosis prevalence in obese patients with T2DM in the VCTE cohort (Supplementary Figure S3A–I, available at https://weekly.chinacdc.cn/). However, no significant difference in the prevalence of MASLD with clinically significant fibrosis was observed between obese and non-obese patients in the liver biopsy cohort (Supplementary Figure S3J–M).

As the number of CMRFs increased, the prevalence of MASLD with clinically significant fibrosis also rose, reaching its peak among patients with five CMRFs (including T2DM) (Supplementary Figure S3N). The prevalence in T2DM patients with additional CMRFs was higher than that in those with

TABLE 1. Baseline characteristics of patients with type 2 diabetes mellitus stratified by obesity status in the VCTE cohort.

Characteristic	Overall (*N*=9,725)	Non-obese (*n*=7,338)	Obese (*n*=2,387)	*P*
Age, years	54.8 (13.82)	56.6 (13.18)	49.4 (14.34)	<0.001
Groups				<0.001
18 to 59 years	5,665 (58.3%)	3,932 (53.6%)	1,733 (72.6%)	
≥60 years	4,060 (41.7%)	3,406 (46.4%)	654 (27.4%)	
Sex, *n* (%)				<0.001
Male	4,865 (50.0%)	3,471 (47.3%)	1,394 (58.4%)	
Female	4,860 (50.0%)	3,867 (52.7%)	993 (41.6%)	
BMI, kg/m^2	25.8 (4.11)	24.0 (2.48)	31.2 (3.33)	<0.001
Waist circumference, cm (*n*=8,101)	89.9 (10.98)	86.5 (8.51)	101.7 (10.41)	<0.001
Hypertension (*n*=8,925)	5,745 (64.4%)	4,292 (62.6%)	1,453 (70.2%)	<0.001
Dyslipidemia (*n*=3,493)	2,374 (67.9%)	1,595 (63.3%)	779 (80.0%)	<0.001
Platelet count, ×10^9/L (*n*=3,492)	237.4 (69.82)	233.2 (68.54)	248.6 (72.05)	<0.001
GGT, IU/L (*n*=2,498)	51.3 (97.28)	48.0 (107.53)	58.3 (69.99)	0.005
ALT, IU/L (*n*=3,802)	38.7 (108.53)	35.1 (123.84)	48.3 (44.95)	<0.001
AST, IU/L (*n*=3,802)	30.2 (77.29)	29.2 (89.11)	32.8 (25.33)	0.054
ALB, g/L (*n*=3,753)	44.5 (4.17)	44.5 (4.23)	44.6 (3.98)	0.566
TBIL, μmol/L (*n*=3,791)	16.1 (12.05)	16.6 (13.42)	14.5 (6.83)	<0.001
Scr, μmol/L (*n*=3,553)	151.2 (1,252.23)	96.7 (700.65)	296.7 (2,101.16)	0.004
UA, μmol/L (*n*=3,545)	356.9 (103.00)	340.4 (95.74)	400.9 (108.60)	<0.001
HbA1c, % (*n*=3,004)	7.1 (1.80)	7.1 (1.80)	7.3 (1.78)	0.007
TC, mmol/L (*n*=3,494)	5.1 (1.27)	5.1 (1.31)	5.1 (1.17)	0.151
TG, mmol/L (*n*=3,494)	2.2 (2.42)	2.0 (2.34)	2.6 (2.55)	<0.001
HDL-C, mmol/L (*n*=3,492)	1.3 (0.33)	1.3 (0.35)	1.2 (0.27)	<0.001
LDL-C, mmol/L (*n*=3,494)	3.0 (3.69)	3.0 (4.32)	3.0 (0.87)	0.894
CAP, dB/m	260.9 (55.77)	250.5 (54.40)	293.1 (46.98)	<0.001
CAP ≥248 dB/m	5,807 (59.7%)	3,783 (51.6%)	2,024 (84.8%)	<0.001
CAP ≥268 dB/m	4,452 (45.8%)	2,736 (37.3%)	1,716 (71.9%)	<0.001
CAP ≥280 dB/m	3,687 (37.9%)	2,205 (30.0%)	1,482 (62.1%)	<0.001
LSM, kPa	6.9 (6.00)	6.5 (5.74)	8.0 (6.60)	<0.001
LSM ≥6.8 kPa	2,972 (30.6%)	1,865 (25.4%)	1,107 (46.4%)	<0.001
LSM ≥8.0 kPa	1,817 (18.7%)	1,096 (14.9%)	721 (30.2%)	<0.001
LSM ≥10.0 kPa	1,020 (10.5%)	613 (8.4%)	407 (17.1%)	<0.001
LSM ≥13.0 kPa	529 (5.4%)	329 (4.5%)	200 (8.4%)	<0.001

Note: Data are presented as mean (SD) or *n* (%).
Abbreviation: VCTE=vibration-controlled transient elastography; ALB=albumin; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; CAP=controlled attenuation parameter; GGT=gamma-glutamyltransferase; HbA1c=hemoglobin A1c; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; LSM=liver stiffness measurement; Scr=serum creatinine; SD=standard deviation; TBIL=total bilirubin; TC=total cholesterol; TG=triglyceride; UA=uric acid.

T2DM alone. In the VCTE cohort, the risk of MASLD with clinically significant fibrosis increased progressively as the number of CMRFs accumulated (Table 3). Among all combinations of T2DM with other CMRFs, T2DM combined with overweight/obesity conferred the highest risk. This association remained statistically significant after adjusting for age and sex.

Multivariate logistic regression analysis identified five independent risk factors for MASLD with clinically significant fibrosis: age, waist circumference, alanine aminotransferase (ALT), total bilirubin (TBIL), and triglyceride (TG). Using these variables, we constructed a non-invasive predictive model for risk

TABLE 2. Baseline characteristics of patients with type 2 diabetes mellitus stratified by obesity status in the liver biopsy cohort.

Characteristic	Overall (*N*=556)	Non-obese (*n*=311)	Obese (*n*=245)	*P*
Age, years	46.6 (12.98)	49.8 (11.69)	42.5 (13.41)	<0.001
Groups				0.001
18 to 59 years	470 (84.5%)	249 (80.1%)	221 (90.2%)	
≥60 years	86 (15.5%)	62 (19.9%)	24 (9.8%)	
Sex, *n* (%)				<0.001
Male	272 (48.9%)	131 (42.1%)	141 (57.6%)	
Female	284 (51.1%)	180 (57.9%)	104 (42.4%)	
BMI, kg/m^2	27.7 (4.14)	24.8 (2.05)	31.4 (3.04)	<0.001
Waist circumference, cm (*n*=393)	95.2 (10.09	89.2 (6.91)	101.9 (8.77)	<0.001
Hypertension (*n*=249)	187 (75.1%)	103 (71.0%)	84 (80.8%)	0.080
Dyslipidemia (*n*=503)	405 (80.5%)	215 (75.7%)	190 (86.8%)	0.002
Platelet count, ×10^9/L	225.5 (65.26)	217.3 (59.69)	235.8 (70.47)	0.001
GGT, IU/L (*n*=387)	89.1 (104.75)	89.6 (112.37)	88.4 (92.40)	0.906
ALT, IU/L	75.4 (58.04)	67.0 (49.52)	86.1 (65.89)	<0.001
AST, IU/L	58.6 (60.39)	53.3 (38.44)	65.3 (79.60)	0.031
ALB, g/L (*n*=551)	43.7 (4.69)	43.5 (4.17)	43.9 (5.29)	0.322
TBIL, μmol/L (*n*=551)	13.3 (6.89)	13.1 (6.92)	13.6 (6.86)	0.337
Scr, μmol/L (*n*=416)	63.4 (15.31)	61.2 (14.97)	66.0 (15.33)	0.001
UA, μmol/L (*n*=414)	364.0 (93.67)	345.7 (92.32)	384.9 (90.99)	<0.001
HbA1c, % (*n*=303)	7.6 (1.80)	7.4 (1.70)	7.8 (1.91)	0.080
TC, mmol/L (*n*=499)	4.9 (1.27)	4.9 (1.25)	5.0 (1.29)	0.396
TG, mmol/L (*n*=499)	2.5 (2.54)	2.3 (2.21)	2.8 (2.88)	0.017
HDL-C, mmol/L (*n*=499)	1.4 (0.96)	1.5 (1.04)	1.3 (0.82)	<0.001
LDL-C, mmol/L (*n*=499)	2.5 (1.09)	2.4 (1.08)	2.7 (1.09)	0.006
CAP, dB/m (*n*=370)	302.7 (42.64)	295.2 (42.88)	313.8 (39.92)	<0.001
LSM, kPa (*n*=368)	10.2 (6.66)	9.7 (6.31)	11.0 (7.08)	0.067
Liver steatosis				0.073
S0	20 (3.6%)	15 (4.8%)	5 (2.0%)	
S1	175 (31.5%)	107 (34.5%)	68 (27.8%)	
S2	235 (42.3%)	124 (40.0%)	111 (45.3%)	
S3	125 (22.5%)	64 (20.6%)	61 (24.9%)	
Liver fibrosis				0.394
F0-F1	297 (53.4%)	173 (55.6%)	124 (50.6%)	
F2	133 (23.9%)	66 (21.2%)	67 (27.3%)	
F3	89 (16.0%)	50 (16.1%)	39 (15.9%)	
F4	37 (6.7%)	22 (7.1%)	15 (6.1%)	

Note: Data are presented as mean (SD) or *n* (%).
Abbreviation: ALB=albumin; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; CAP=controlled attenuation parameter; GGT=gamma-glutamyltransferase; HbA1c=hemoglobin A1c; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; LSM=liver stiffness measurement; Scr=serum creatinine; SD=standard deviation; TBIL=total bilirubin; TC=total cholesterol; TG=triglyceride; UA=uric acid.

stratification of MASLD with clinically significant fibrosis in obese patients with T2DM, expressed by the following formula:

$$\text{Model} = -10.983 + 0.025 \times \text{Age (years)} + 0.074 \times$$

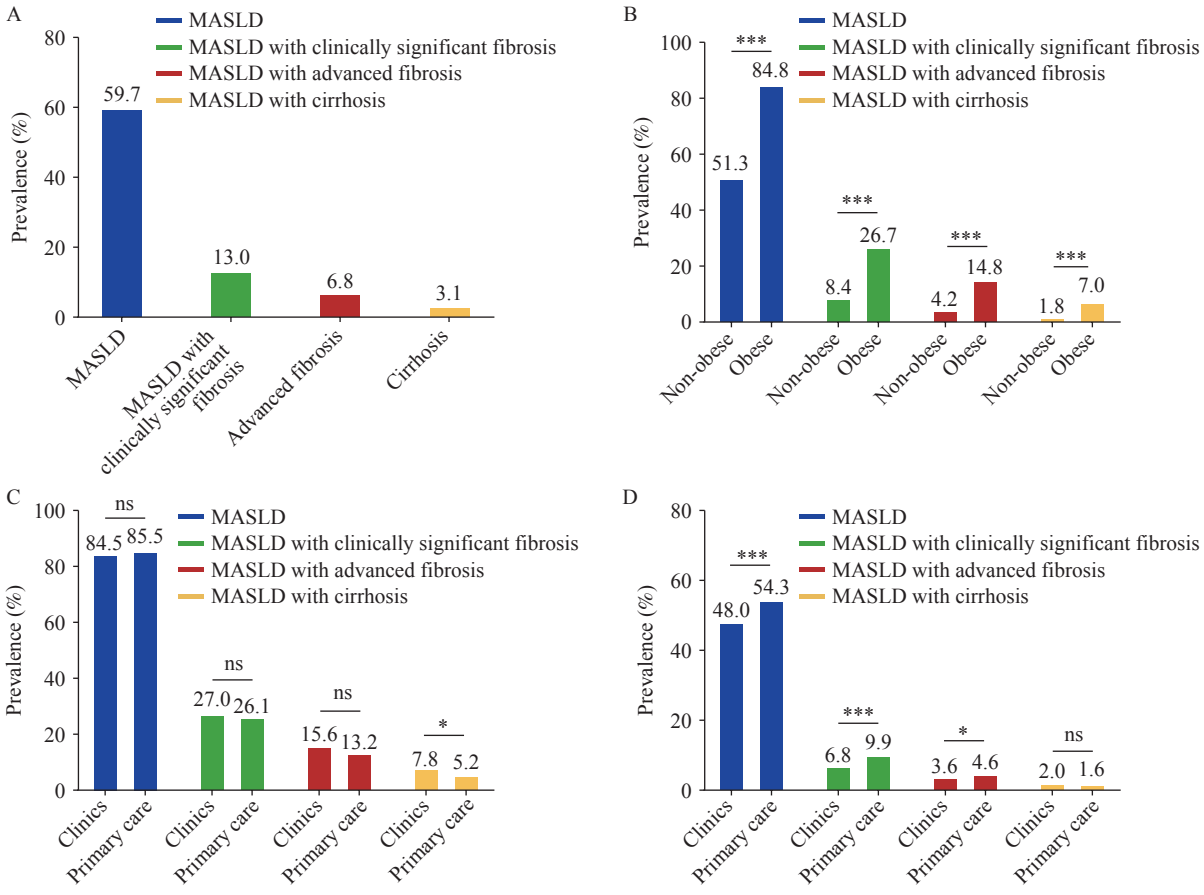

FIGURE 1. Prevalence of MASLD and liver fibrosis stages among patients with type 2 diabetes mellitus. (A) Overall prevalence across all patients; (B) Comparison between obese and non-obese patient groups; (C) Comparison within obese patients: clinic-based versus primary care settings; (D) Comparison within non-obese patients: clinic-based versus primary care settings.
* *P*<0.05; *** *P*<0.001; ns, not significant.
Abbreviation: MASLD=metabolic dysfunction-associated steatotic liver disease.

waist circumference (cm) + 0.015 × ALT (IU/L) – 0.076 × TBIL (μmol/L) + 0.223 × TG (mmol/L)

The model demonstrated robust discriminatory performance, with an area under the receiver operating characteristic curve of 0.799 (95% *CI*: 0.767–0.832). A cutoff value of –2.197 achieved ≥95% sensitivity for excluding clinically significant fibrosis, whereas a cutoff of 0.405 achieved ≥95% specificity for confirming clinically significant fibrosis.

DISCUSSION

This large-scale, multicenter prospective study represents the first comprehensive assessment of MASLD with clinically significant fibrosis prevalence and associated risk factors among patients with T2DM in China. Our findings revealed that 59.7% of T2DM patients had MASLD, and 13.0% had clinically significant fibrosis, with the prevalence increasing progressively with rising BMI. Notably, obese patients with T2DM exhibited a substantially higher prevalence of MASLD with clinically significant fibrosis compared to their non-obese counterparts (26.7% *vs.* 8.4%, *P*<0.001). Furthermore, the prevalence escalated with accumulating CMRFs, with the combination of T2DM and overweight/obesity conferring the greatest risk. Additionally, our non-invasive predictive model incorporating age, waist circumference, ALT, TBIL, and TG demonstrated robust diagnostic performance for identifying clinically significant fibrosis.

Our previous research characterized the bidirectional relationship between T2DM and MASLD (*5*). Younossi et al. (*6*) reported pooled all-cause and liver-specific mortality rates of 16.79 and 2.15 per 1,000 person-years, respectively, among MASLD patients with T2DM. In comparison, our study identified a MASLD prevalence of 59.7% in T2DM patients,

TABLE 3. Logistic regression analyses evaluating associations between cardiometabolic risk factors and MASLD with clinically significant fibrosis in the VCTE and liver biopsy cohorts.

Characteristic	VCTE cohort			Liver biopsy cohort		
	OR	95% *CI*	*P*	*OR*	95% *CI*	*P*
Number of CMRF(s) (unadjusted)						
1 CMRF (only T2DM)	Reference					
T2DM + Any 1 CMRF	1.87	1.15–3.05	0.012	3.54	1.49–8.44	0.004
T2DM + Any 2 CMRFs	2.46	1.54–3.93	<0.001	2.77	1.18–6.54	0.020
T2DM + Any 3 CMRFs	3.35	2.10–5.34	<0.001	2.67	1.14–6.24	0.023
T2DM + 4 CMRFs	4.19	2.52–6.96	<0.001	2.13	0.85–5.35	0.108
Number of CMRF(s) (age- and sex-adjusted)						
1 CMRF (only T2DM)	Reference					
T2DM + Any 1 CMRF	1.87	1.15–3.05	0.012	3.52	1.46–8.46	0.005
T2DM + Any 2 CMRFs	2.44	1.53–3.90	<0.001	2.78	1.17–6.63	0.021
T2DM + Any 3 CMRFs	3.31	2.07–5.27	<0.001	2.77	1.17–6.54	0.020
T2DM + 4 CMRFs	4.09	2.46–6.82	<0.001	2.22	0.87–5.69	0.095

Abbreviation: *CI*=confidence interval; CMRF=cardiometabolic risk factor; MASLD=metabolic dysfunction-associated steatotic liver disease; *OR*=odds ratio; T2DM=type 2 diabetes mellitus; VCTE=vibration-controlled transient elastography.

slightly lower than the 65.04% reported by a recent meta-analysis (*7*). These discrepancies likely reflect variations in diagnostic methodologies, population demographics, and study inclusion criteria. Specifically, differences in imaging modalities (ultrasound versus VCTE), ethnic composition, and metabolic disease severity across cohorts may contribute to the observed variations. Nevertheless, the prevalence remains substantial, underscoring the critical need for systematic liver disease screening in this high-risk population.

MASLD with clinically significant fibrosis represents a pivotal disease stage associated with elevated risks of cirrhosis, hepatocellular carcinoma, and liver-related mortality (*2*). The recent ADA consensus report recommended routine assessment for MASLD and liver fibrosis in T2DM patients with obesity (*2*). In our cohort, the prevalence of MASLD with clinically significant fibrosis was 13.0% among all T2DM patients and 26.7% among those with obesity, highlighting the strong association between adiposity and hepatic fibrosis progression. By comparison, Cho et al. (*7*) reported a higher prevalence of 35.54%. This discrepancy likely reflects the more severe disease spectrum in meta-analyses that predominantly included patients referred for specialist evaluation rather than population-based cohorts. Our findings emphasize that obesity, regardless of the anthropometric measurement used, substantially increases the burden of clinically significant fibrosis in T2DM patients.

Obesity serves as a critical driver of liver disease progression in patients with T2DM and MASLD (*8*). Our sensitivity analyses employing multiple obesity definitions, including BMI, waist circumference, waist-hip ratio, and waist-height ratio, revealed varying prevalence estimates of MASLD with clinically significant fibrosis, ranging from 14.4% to 26.7% in the VCTE cohort and from 29.6% to 49.4% in the liver biopsy cohort. These findings underscore the substantial liver disease burden associated with excess adiposity, regardless of the anthropometric measurement used. Moreover, they suggest that simple anthropometric indices beyond BMI may offer additional insights into metabolic risk and fibrosis burden in patients with T2DM and obesity (*9*).

CMRFs, such as hypertension, dyslipidemia, and obesity, demonstrated strong associations with MASLD with clinically significant fibrosis (*3*,*10*). The prevalence of clinically significant fibrosis increased progressively with the accumulation of CMRFs, even after adjusting for age and sex, suggesting additive or potentially synergistic effects. Notably, the combination of T2DM with overweight or obesity conferred the highest risk among all CMRF combinations, emphasizing the interconnected pathophysiology of metabolic dysfunction and liver disease. Furthermore, sex, waist circumference, AST,

ALB, TBIL, and HbA1c emerged as independent risk factors for clinically significant fibrosis, with restricted cubic spline analyses revealing non-linear associations with liver fibrosis risk.

This study demonstrates several notable strengths. First, it represents one of the largest multicenter prospective investigations assessing the prevalence of MASLD with clinically significant fibrosis in Chinese patients with T2DM, thereby providing robust and generalizable estimates. Second, we employed both VCTE, a widely validated non-invasive assessment tool, and liver biopsy, the gold standard for fibrosis diagnosis, thereby minimizing diagnostic misclassification. Third, we conducted comprehensive sensitivity analyses using multiple obesity definitions to validate the consistency of our findings across different anthropometric measures. Finally, we developed a novel non-invasive model that may facilitate risk stratification for clinically significant fibrosis in this high-risk population.

However, several limitations warrant consideration. First, blood sample data were incomplete for some patients, and information on medication use (e.g., antidiabetic, lipid-lowering, or hepatoprotective agents) was unavailable, potentially introducing residual confounding. Additionally, incomplete laboratory data may have modestly reduced the accuracy and generalizability of our prediction model. Future studies incorporating more comprehensive data collection are needed to validate our findings. Second, VCTE accuracy may be compromised in patients with severe obesity, potentially introducing measurement bias in LSM values. Nevertheless, our subgroup analysis stratified by BMI demonstrated generally consistent results across obesity categories. Finally, the cross-sectional design precludes causal inference regarding the observed associations between metabolic variables and liver fibrosis. Longitudinal studies are warranted to establish temporal relationships and validate the proposed risk stratification model.

In conclusion, our study demonstrates a high prevalence of MASLD with clinically significant fibrosis among T2DM patients, particularly those with obesity and multiple CMRFs. These findings underscore the critical importance of routine liver fibrosis screening and integrated management of metabolic risk factors to mitigate liver-related complications in this high-risk population.

Conflicts of interest: No conflicts of interest.

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Ethical statement: Conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The Ethics Committee of Zhongda Hospital, Medical School, Southeast University, approved the study protocol (approval number: 2024ZDSYLL398-P01). All participants provided written informed consent prior to enrollment.

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REFERENCES

1. Younossi ZM, Kalligeros M, Henry L. Epidemiology of metabolic dysfunction-associated steatotic liver disease. Clin Mol Hepatol 2025;31 (S1):S32 – 50. https://doi.org/10.3350/cmh.2024.0431.
2. Cusi K, Abdelmalek MF, Apovian CM, Balapattabi K, Bannuru RR, Barb D, et al. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in people with diabetes: the need for screening and early intervention. A consensus report of the American diabetes association. Diabetes Care 2025;48(7):1057 – 82. https://doi.org/10.2337/dci24-0094.
3. Shang Y, Grip ET, Modica A, Skröder H, Ström O, Ntanios F, et al. Metabolic syndrome traits increase the risk of major adverse liver outcomes in type 2 diabetes. Diabetes Care 2024;47(6):978 – 85. https://doi.org/10.2337/dc23-1937.
4. Liu SH, Wan H, Yang L, Shen J, Qi XL. High prevalence of steatotic liver disease and fibrosis in the general population: a large prospective study in China. J Hepatol 2025;82(1):e23 – 5. https://doi.org/10.1016/j.jhep.2024.07.026.
5. Qi XL, Li J, Caussy C, Teng GJ, Loomba R. Epidemiology, screening, and co-management of type 2 diabetes mellitus and metabolic dysfunction-associated steatotic liver disease. Hepatology 2024. http://dx.doi.org/10.1097/HEP.0000000000000913
6. Younossi ZM, Golabi P, Price JK, Owrangi S, Gundu-Rao N, Satchi R, et al. The global epidemiology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among patients with type 2 diabetes. Clin Gastroenterol Hepatol 2024;22(10):1999 – 2010.e8. https://doi.org/10.1016/j.cgh.2024.03.006.
7. En Li Cho E, Ang CZ, Quek J, Fu CE, Lim LKE, Heng ZEQ, et al. Global prevalence of non-alcoholic fatty liver disease in type 2 diabetes mellitus: an updated systematic review and meta-analysis. Gut 2023;72 (11):2138 – 48. https://doi.org/10.1136/gutjnl-2023-330110.
8. American Diabetes Association Professional Practice Committee. 8. Obesity and weight management for the prevention and treatment of type 2 diabetes: standards of care in diabetes-2025. Diabetes Care 2025;48(1 Suppl 1):S167-80. http://dx.doi.org/10.2337/dc25-S008.
9. Rubino F, Cummings DE, Eckel RH, Cohen RV, Wilding JPH, Brown WA, et al. Definition and diagnostic criteria of clinical obesity. Lancet Diabetes Endocrinol 2025;13(3):221 – 62. https://doi.org/10.1016/S2213-8587(24)00316-4.
10. Park H, Cheuk-Fung Yip T, Yoon EL, Lai-Hung Wong G, Lee HS, Wai-Sun Wong V, et al. Impact of cardiometabolic risk factors on hepatic fibrosis and clinical outcomes in MASLD: a population-based multi-cohort study. JHEP Rep 2025;7(6):101388. https://doi.org/10.1016/j.jhepr.2025.101388.

SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Distribution of the data.

No.	City	Sample size	
		VCTE cohort (*n*=9,725)	Biopsy cohort (*n*=556)
01	Baotou	222	–
02	Bozhou	543	–
03	Hangzhou	–	53
04	Huozhou	1,198	–
05	Jinhua	736	–
06	Lishui	57	–
07	Nanjing	1,242	–
08	Ningxia	166	–
09	Ningbo	–	51
10	Qiqihar	279	–
11	Qingdao	173	2
12	Shanghai	39	167
13	Shenyang	1,164	87
14	Shiyan	210	–
15	Shunde	1,359	–
16	Suining	94	–
17	Wenzhou	–	194
18	Wuwei	10	–
19	Xingtai	989	–
20	Zhengzhou	765	2
21	Zhuhai	479	–

Note: "–" means data was not available.
Abbreviation: VCTE=vibration-controlled transient elastography.

Exclusion Criteria

Patients were excluded if they met any of the following criteria: 1) type 1 diabetes mellitus (DM); 2) gestational DM; 3) other specific types of DM; 4) missing body mass index (BMI) data; 5) alcohol consumption exceeding 20 g/day (females) or 30 g/day (males); 6) inability to undergo vibration-controlled transient elastography (VCTE) or liver biopsy; 7) an interval exceeding one month between VCTE or liver biopsy and blood sample collection.

Vibration-controlled Transient Elastography and Liver Biopsy Assessment

Trained operators, blinded to participants' clinical and laboratory data, performed VCTE using FibroScan with M and XL probes following standardized protocols (*1*). Examinations were deemed reliable when ≥10 valid measurements were obtained with an interquartile range/median ratio <30%. Histological slides were evaluated at each participating center according to standard procedures (*2*) by pathologists who remained blinded to all clinical information.

Logistic Regression Analyses

We employed logistic regression analyses to evaluate associations between cardiometabolic risk factors (CMRFs) and metabolic dysfunction-associated steatotic liver disease (MASLD) with clinically significant fibrosis, as well as to identify independent risk factors for this condition. Variables demonstrating P values <0.05 in univariate analyses were subsequently entered into multivariate models. Missing data were handled through multiple imputation, generating five datasets with a seed value of 1,234.

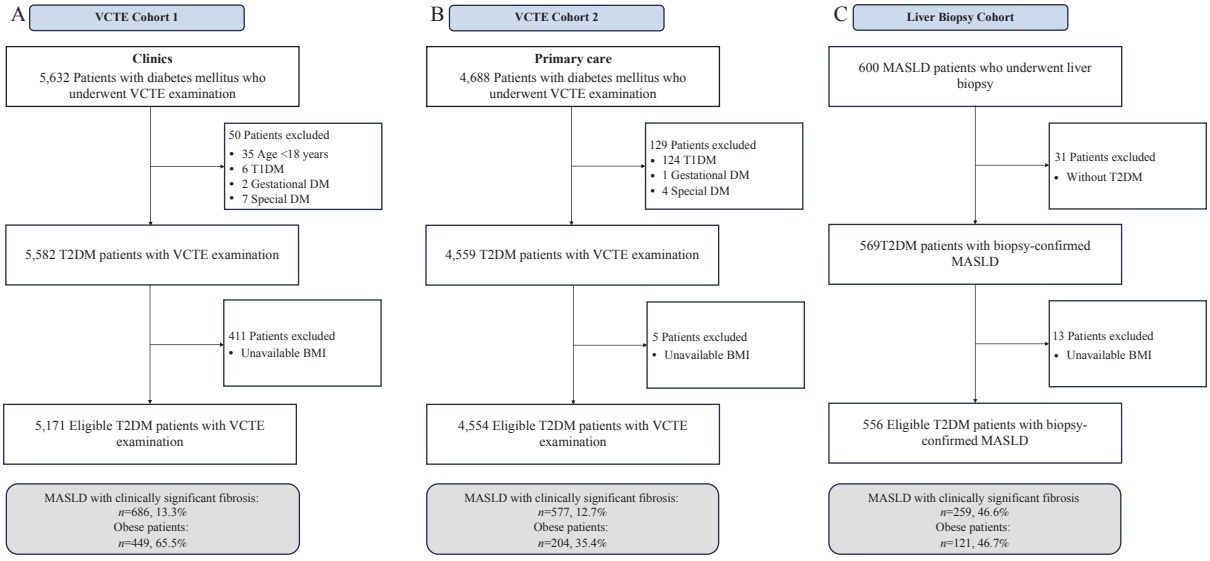
SUPPLEMENTARY TABLE S2. Baseline characteristics of patients with type 2 diabetes mellitus stratified by clinical setting.

Characteristic	Clinics (*n*=5,171)	Primary care (*n*=4,554)	*P*
Age, years	49.0 (13.87)	61.4 (10.39)	<0.001
Groups			<0.001
18 to 59 years	3,867 (74.8%)	1,798 (39.5%)	
≥60 years	1,304 (25.2%)	2,756 (60.5%)	
Sex, *n* (%)			<0.001
Male	3,180 (61.5%)	1,685 (37.0%)	
Female	1,991 (38.5%)	2,869 (63.0%)	
BMI, kg/m^2	26.5 (14.53)	25.0 (13.38)	<0.001
Groups			<0.001
≥28.0 kg/m²	1,629 (31.5%)	758 (16.6%)	
<28.0 kg/m²	3,542 (68.5%)	3,796 (83.4%)	
Waist circumference, cm (*n*=8,101)	92.6 (11.94)	87.9 (9.66)	<0.001
Hypertension (*n*=8,925)	2,240 (51.0%)	3,505 (77.4%)	<0.001
Dyslipidemia (*n*=3,494)	1,569 (71.3%)	805 (62.3%)	<0.001
Platelet count, ×10^9/L (*n*=3,492)	226.2 (68.73)	256.4 (67.56)	<0.001
GGT, IU/L (*n*=2,498)	51.3 (97.28)	–	–
ALT, IU/L (*n*=3,802)	43.7 (132.56)	28.9 (19.93)	<0.001
AST, IU/L (*n*=3,802)	32.8 (94.71)	25.1 (11.14)	<0.001
ALB, g/L (*n*=3,753)	43.7 (4.59)	46.2 (2.48)	<0.001
TBIL, μmol/L (*n*=3,791)	16.2 (14.15)	15.8 (6.22)	0.205
Scr, μmol/L (*n*=3,553)	195.7 (1,568.39)	73.4 (23.14)	<0.001
UA, μmol/L (*n*=3,545)	352.5 (100.64)	364.7 (106.59)	<0.001
HbA1c, % (*n*=3,004)	7.4 (2.03)	6.7 (1.32)	<0.001
TC, mmol/L (*n*=3,494)	4.9 (1.27)	5.5 (1.17)	<0.001
TG, mmol/L (*n*=3,494)	2.2 (2.53)	2.1 (2.21)	0.099
HDL-C, mmol/L (*n*=3,492)	1.2 (0.32)	1.4 (0.33)	<0.001
LDL-C, mmol/L (*n*=3,494)	2.9 (4.61)	3.1 (0.80)	0.101
CAP, dB/m	260.7 (55.27)	261.2 (56.35)	0.647
CAP ≥248 dB/m	3,088 (59.7%)	2,719 (59.7%)	0.990
CAP ≥268 dB/m	2,377 (46.0%)	2,075 (45.6%)	0.690
CAP ≥280 dB/m	1,977 (38.2%)	1,710 (37.5%)	0.488
LSM, kPa	7.4 (7.59)	6.3 (3.29)	<0.001
LSM ≥6.8 kPa	1,602 (31.0%)	1,370 (30.1%)	0.338
LSM ≥8.0 kPa	1,051 (20.3%)	766 (16.8%)	<0.001
LSM ≥10.0 kPa	666 (12.9%)	354 (7.8%)	<0.001
LSM ≥13.0 kPa	399 (7.7%)	130 (2.9%)	*P*<0.001

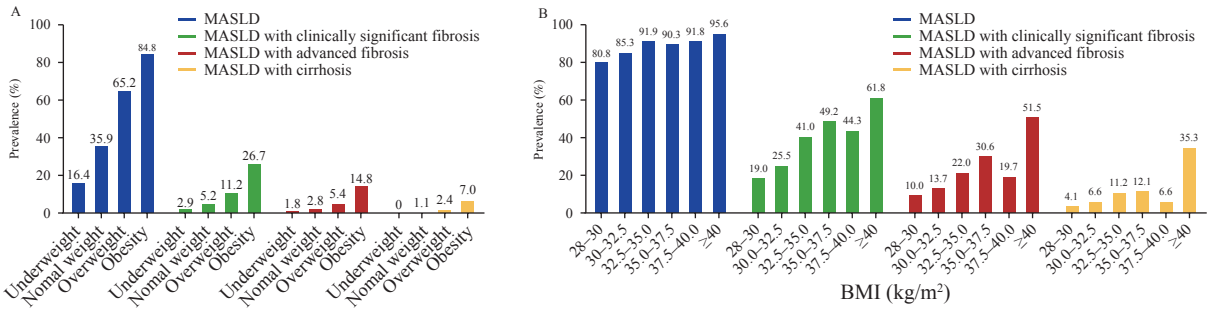
Note: Data are presented as mean (SD) or *n* (%).
Abbreviation: ALB=albumin; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BMI=body mass index; CAP=controlled attenuation parameter; GGT=gamma-glutamyltransferase; HbA1c=hemoglobin A1c; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; LSM=liver stiffness measurement; Scr=serum creatinine; SD=standard deviation; TBIL=total bilirubin; TC=total cholesterol; TG=triglyceride; UA=uric acid.

Sensitivity Analyses

To validate the robustness of our findings, we conducted sensitivity analyses using alternative obesity definitions: waist circumference, waist-to-hip ratio (WHR), and waist-to-height ratio (WHTR). These analyses confirmed the



SUPPLEMENTARY FIGURE S1. Study flow diagram.
Abbreviation: MASLD=metabolic dysfunction-associated steatotic liver disease; T2DM=type 2 diabetes mellitus; VCTE=vibration-controlled transient elastography.



SUPPLEMENTARY FIGURE S2. Prevalence of MASLD with clinically significant fibrosis among patients with type 2 diabetes mellitus in the VCTE cohort. (A) Prevalence in patients with T2DM stratified by BMI categories; (B) Prevalence in obese patients with T2DM according to different BMI cutoff values.
Abbreviation: BMI=body mass index; MASLD=metabolic dysfunction-associated steatotic liver disease; T2DM=type 2 diabetes mellitus; VCTE=vibration-controlled transient elastography.

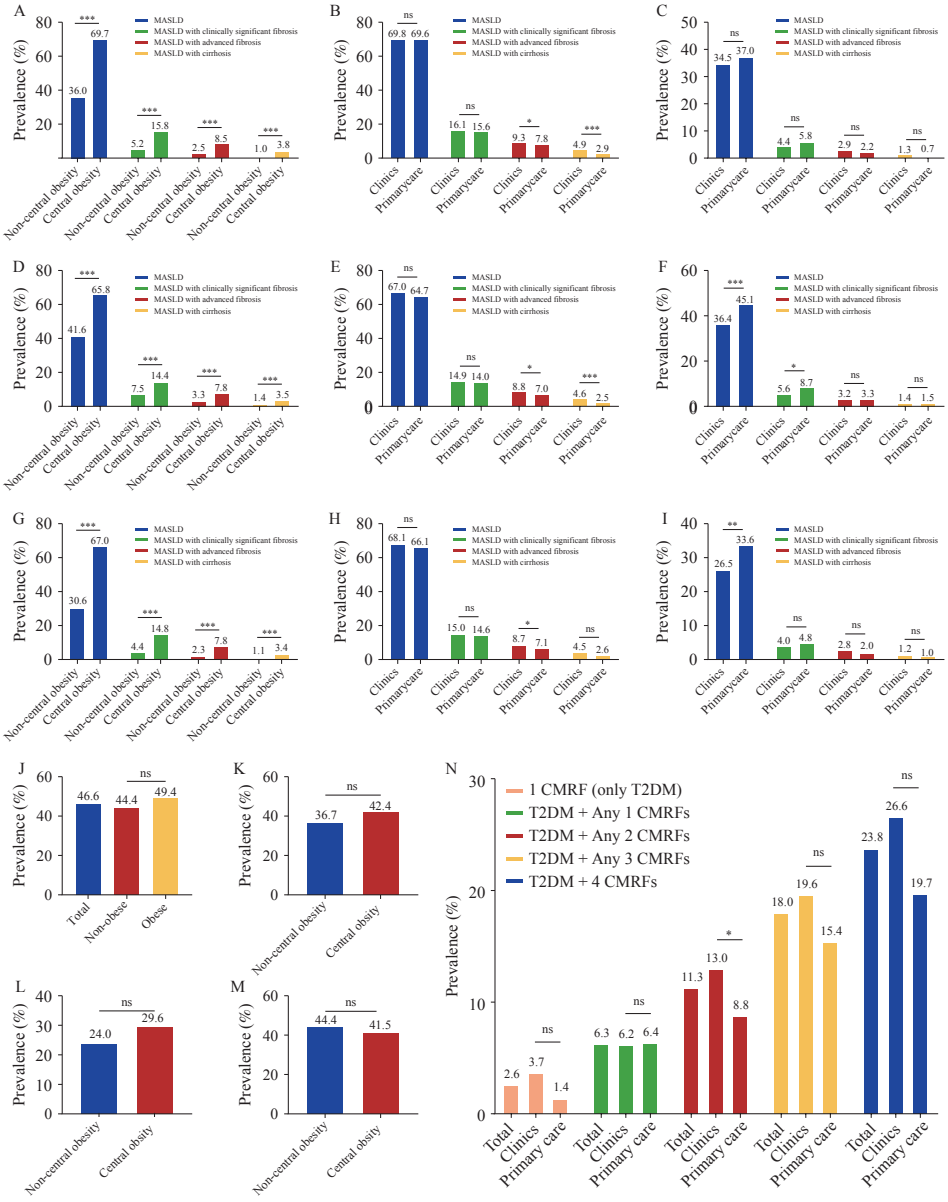
consistently elevated prevalence of MASLD with clinically significant fibrosis among patients with type 2 diabetes mellitus (T2DM). Additionally, we stratified prevalence estimates across different obesity classes using established cutoff values (*3*).

Statistical Analyses

Continuous variables are expressed as mean (SD), and categorical variables as n (%). Group differences were assessed using the chi-square test or Fisher's exact test for categorical variables, and Student's *t*-test or Mann-Whitney *U* test for continuous variables. A two-tailed $P<0.05$ was considered statistically significant.

Definitions

In the VCTE cohort, advanced fibrosis was defined as liver stiffness measurement (LSM) ≥10 kPa, and cirrhosis as LSM ≥13 kPa (*4*). Liver steatosis was identified as controlled attenuation parameter (CAP) ≥248 dB/m (*5*). Body mass index (BMI) categories were defined as follows: underweight <18.5 kg/m^2, normal weight 18.5–23.9 kg/m^2, overweight 24.0–27.9 kg/m^2, and obesity ≥28 kg/m^2 (*6*). Central obesity was identified as waist circumference ≥90 cm (males) or ≥80 cm (females)(*5*), waist-to-hip ratio (WHR) >0.9 (males) or >0.85 (females) (*7*), or waist-to-



SUPPLEMENTARY FIGURE S3. Prevalence of MASLD with clinically significant fibrosis among patients with type 2 diabetes mellitus. (A) Central obesity versus non-central obesity defined by waist circumference in the VCTE cohort; (B) Central obesity defined by waist circumference in the VCTE cohort: clinic-based versus primary care settings; (C) Non-central obesity defined by waist circumference in the VCTE cohort: clinic-based versus primary care settings; (D) Central obesity versus non-central obesity defined by waist-to-hip ratio in the VCTE cohort; (E) Central obesity defined by waist-to-hip ratio in the VCTE cohort: clinic-based versus primary care settings; (F) Non-central obesity defined by waist-to-hip ratio in the VCTE cohort: clinic-based versus primary care settings; (G) Central obesity versus non-central obesity defined by waist-to-height ratio in the VCTE cohort; (H) Central obesity defined by waist-to-height ratio in the VCTE cohort: clinic-based versus primary care settings; (I) Non-central obesity defined by waist-to-height ratio in the VCTE cohort: clinic-based versus primary care settings; (J) Obesity versus non-obesity defined by body mass index in the liver biopsy cohort; (K) Central obesity versus non-central obesity defined by waist circumference in the liver biopsy cohort; (L) Central obesity versus non-central obesity defined by waist-to-hip ratio in the liver biopsy cohort; (M) Central obesity versus non-central obesity defined by waist-to-height ratio in the liver biopsy cohort; (N) Prevalence stratified by the cumulative number of cardiometabolic risk factors.

Note: ns, no significance.

Abbreviations: BMI=body mass index; CMRFs=cardiometabolic risk factors; MASLD=metabolic dysfunction-associated steatotic liver disease; VCTE=vibration-controlled transient elastography; WC=waist circumference; WHR=waist-to-hip ratio; WHTR=waist-to-height ratio.

* P<0.05; ** P<0.01 *** P<0.001.

height ratio (WHTR) ≥0.5 (*8*).

Hypertension was defined as blood pressure ≥130/80 mmHg (*9*). Elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels were defined as >40 IU/L (*10*). Dyslipidemia was diagnosed based on the following criteria: total cholesterol ≥6.22 mmol/L, triglycerides ≥1.70 mmol/L, high-density lipoprotein cholesterol <1.04 mmol/L for males or <1.30 mmol/L for females, or low-density lipoprotein cholesterol ≥4.14 mmol/L (*11*). Cardiometabolic risk factors included overweight or obesity, dysglycemia or T2DM, elevated triglycerides, reduced high-density lipoprotein cholesterol, and elevated blood pressure (*5*).

REFERENCES

1. de Lédinghen V, Vergniol J. Transient elastography (FibroScan). Gastroentérol Clin Biol 2008;32(6 Suppl 1):58-67. http://dx.doi.org/10.1016/S0399-8320(08)73994-0.
2. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD. Liver biopsy. Hepatology 2009;49(3):1017 – 44. https://doi.org/10.1002/hep.22742.
3. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363(9403):157 – 63. https://doi.org/10.1016/S0140-6736(03)15268-3.
4. Liu SH, Wan H, Yang L, Shen J, Qi XL. High prevalence of steatotic liver disease and fibrosis in the general population: a large prospective study in China. J Hepatol 2025;82(1):e23 – 5. https://doi.org/10.1016/j.jhep.2024.07.026.
5. European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol 2024;81(3):492 – 542. https://doi.org/10.1016/j.jhep.2024.04.031.
6. Wang LM, Peng W, Zhao ZP, Zhang M, Shi ZM, Song ZW, et al. Prevalence and treatment of diabetes in China, 2013-2018. JAMA 2021;326(24):2498 – 506. https://doi.org/10.1001/jama.2021.22208.
7. Zhang YB, Chen GC, Sotres-Alvarez D, Perreira KM, Daviglus ML, Pirzada A, et al. General or central obesity and mortality among US Hispanic and Latino adults. JAMA Netw Open 2024;7(1):e2351070. https://doi.org/10.1001/jamanetworkopen.2023.51070.
8. Abeysekera KWM, Fernandes GS, Hammerton G, Portal AJ, Gordon FH, Heron J, et al. Prevalence of steatosis and fibrosis in young adults in the UK: a population-based study. Lancet Gastroenterol Hepatol 2020;5(3):295 – 305. https://doi.org/10.1016/S2468-1253(19)30419-4.
9. American Diabetes Association Professional Practice Committee. 10. Cardiovascular disease and risk management: standards of care in diabetes-2025. Diabetes Care 2025;48(1 Suppl 1):S207-38. http://dx.doi.org/10.2337/dc25-S010.
10. Man SLM, Deng YH, Ma Y, Fu JZ, Bao HL, Yu CQ, et al. Prevalence of liver steatosis and fibrosis in the general population and various high-risk populations: a nationwide study with 5. 7 million adults in China. Gastroenterology 2023;165(4):1025 – 40. https://doi.org/10.1053/j.gastro.2023.05.053.
11. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001;285(19):2486 – 97. https://doi.org/10.1001/jama.285.19.2486.